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(54) Title: METHODS AND DEVICES FOR THE REMOVAL OF PSORALENS FROM BLOOD PRODUCTS

(57) Abstract

Methods and devices for the removal of psoralens and psoralen photoproducts from blood products are described. The methods include contacting a psoralen- and irradiation-treated blood product with a resin capable of adsorbing psoralens and psoralen photoproducts. The removal process is particularly suitable for use with platelet concentrates and plasma because the process does not have a significant adverse effect on clotting factor function. The methods and devices can be incorporated with apheresis systems and other devices and procedures currently used to process blood products for transfusion.

I claim:

1. A method of inactivating nucleic acid-containing pathogens in blood products, comprising:

a) providing, in any order: i) psoralen, ii) photoactivation means, iii) a blood product intended for *in vivo* use suspected of being contaminated with said pathogens;

b) adding said psoralen to said blood product to create a solution of psoralen at a concentration;

c) treating said solution with said photoactivation means so as to create a treated blood product wherein said pathogens are inactivated and wherein at least a portion of said psoralen concentration is free in said solution; and

d) removing substantially all of said portion of said psoralen concentration free in solution in said treated blood product.

2. The method of Claim 1, wherein said removing comprises contacting said treated blood product with a resin.

3. The method of Claim 2, wherein said resin is adsorbent.

4. The method of Claim 3, wherein said resin comprises polystyrene.

5. The method of Claim 3, wherein said resin comprises polyacrylic ester.

6. The method of Claim 3, wherein said resin comprises activated charcoal.

7. The method of Claim 2, wherein said contacting comprises perfusing said blood product through an in-line column containing said resin

8 The method of Claim 2, wherein said contacting occurs within a bag containing said resin

enclosure in said bag, said mesh enclosure adapted to allow said blood product to contact said resin.

10. The method of Claim 9, further comprising a partition mounted external to, and in contact with, said bag, said partition adapted to separate said blood product from said mesh enclosure and adapted to be removed from said bag at a predetermined time.

11. The method of Claim 1, wherein said psoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

12. The method of Claim 1, wherein said blood product comprises platelets.

13. The method of Claim 1, wherein said blood product comprises plasma.

14. A blood decontamination system, comprising a first blood bag and an in-line column containing resin capable of removing psoralen, said in-line column having an input end in fluidic communication with said first blood bag, an output end, and a capacity.

15. The system of Claim 14, wherein said output end is in fluidic contact with a second blood bag.

16. The system of Claim 15, further comprising a flow adapter positioned in fluidic contact with said in-line column and positioned after said output end of said in-line column and before said second bag.

17. The system of Claim 14, wherein said resin is adsorbent.

18. A blood bag, comprising:

a) a biocompatible housing; and

b) a compartment within said housing containing a resin capable of removing psoralen

20. The blood bag of Claim 18, further comprising a mesh enclosure disposed within said compartment and containing said resin, said mesh enclosure adapted to allow a blood product to contact said resin.

21. The blood bag of Claim 20, further comprising a partition mounted external to, and in contact with, said biocompatible housing, said partition adapted to separate said blood product from said mesh enclosure and to be removed from said bag at a predetermined time to allow said blood product to contact said resin.

22. The blood bag of Claim 18, wherein said resin is adsorbent.

23. A method of inactivating nucleic acid-containing pathogens in blood products, comprising:

a) providing, in any order: i) a donor, said donor capable of providing blood suspected of being contaminated with said pathogens, ii) blood separation means for separating said blood into blood products, iii) psoralen, iv) photoactivation means, and v) psoralen removal means;

b) withdrawing said blood from said donor and introducing said blood into said blood separation means;

c) isolating a blood product from said blood with said blood separation means;

d) adding said psoralen to said blood product to create a solution of psoralen at a concentration;

e) treating said solution with said photoactivation means so as to create a treated blood product wherein said pathogens are inactivated and wherein at least a portion of said psoralen concentration is free in said solution; and

f) removing substantially all of said portion of said psoralen free in solution in said treated blood product with said psoralen removal means.

24. The method of Claim 23, wherein said blood separation means is an apheresis system.

26. The method of Claim 23, wherein said blood product is plasma.

27. The method of Claim 23, wherein said psoralen removal means comprises a mesh enclosure containing a resin, said mesh enclosure adapted to allow a blood product to contact said resin.

28. The method of Claim 27, wherein said resin is adsorbent.

29. The method of Claim 28, wherein said resin comprises a polymer.

30. The method of Claim 23, wherein said psoralen is an aminopsoralen.

31. The method of Claim 30, wherein said aminopsoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

32. The method of Claim 23, wherein said psoralen is a brominated psoralen.

33. A method of inactivating nucleic acid-containing pathogens in blood products, comprising:

a) providing, in any order: i) a donor, said donor capable of providing blood suspected of being contaminated with said pathogens, ii) an apheresis system for separating platelets from said blood, iii) synthetic media, iv) a platelet collection container, v) 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen, vi) photoactivation means, and vii) psoralen removal means;

b) withdrawing said blood from said donor and introducing said blood into said apheresis system;

c) isolating said platelets from said blood with said apheresis system;

d) collecting said platelets in a platelet container over a period of time;

e) adding said synthetic media to said platelets in said platelet container, thereby producing a platelet mixture comprising platelets and synthetic media.

platelet mixture to create a solution of 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen at a concentration;

g) treating said solution with said photoactivation means so as to create a treated platelet mixture wherein said pathogens are inactivated and wherein at least a portion of said 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen concentration is free in said solution; and

h) removing substantially all of said portion of said 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen free in solution in said treated platelet mixture with said psoralen removal means.

34. The method of Claim 33, wherein said synthetic media comprises phosphate.

35. The method of Claim 33, wherein said psoralen removal means comprises a mesh enclosure containing a resin, said mesh enclosure adapted to allow a platelet mixture to contact said resin.

36. The method of Claim 35, wherein said resin is adsorbent.

37. The method of Claim 36, wherein said resin comprises a polymer.

38. The method of Claim 37, wherein said polymer comprises polystyrene.

39. A container for a blood product, comprising:

a) a biocompatible housing;

b) a resin capable of removing psoralen from said blood product, said resin contained within said biocompatible housing; and

c) means for retaining said resin within said biocompatible housing.

40. The container of Claim 39, wherein said retaining means comprises a mesh enclosure disposed within said biocompatible housing, said mesh enclosure containing said resin and adapted to allow a blood product to contact said resin

42. The container of Claim 41, wherein said retaining means comprises a mesh filter positioned in said inlet/oulet line and in fluidic communication with said biocompatible housing.

43. The container of Claim 39, wherein said resin is adsorbent.

44. The container of Claim 39, wherein said psoralen is an aminopsoralen.

45. The container of Claim 44, wherein said aminopsoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

46. A method of inactivating nucleic acid-containing pathogens in blood products, comprising:

a) providing, in any order: i) psoralen, ii) photoactivation means, iii) a first container containing a blood product intended for *in vivo* use suspected of being contaminated with said pathogens;

b) adding said psoralen to said blood product in said first container to create a solution of psoralen at a concentration;

c) treating said solution with said photoactivation means so as to create a treated blood product wherein said pathogens are inactivated and wherein at least a portion of said psoralen concentration is free in said solution; and

d) removing some of said portion of said psoralen free in solution in said treated blood product.

47. The method of Claim 46, wherein said psoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

48. The method of Claim 46, wherein said psoralen is brominated.

49 The method of Claim 48, wherein said brominated psoralen is 5-bromo-8-methoxypsoralen

(diethylaminopropyloxy)-psoralen.

51. The method of Claim 46, wherein said psoralen is a quaternary amine.

52. The method of Claim 51, wherein said quaternary amine psoralen is 4'-(triethylamino) methyl-4,5',8-trimethylpsoralen.

53. The method of Claim 46, wherein said removing step comprises transferring said treated blood product into a second container, comprising: i) a biocompatible housing; ii) a resin capable of removing psoralen from said blood product, said resin contained within said biocompatible housing; and iii) retaining means for retaining said resin within said biocompatible housing under conditions such that some of said portion of said psoralen concentration free in solution is removed from said treated blood product.

54. The method of Claim 53, wherein said retaining means comprises a mesh enclosure disposed within said biocompatible housing, said mesh enclosure containing said resin and adapted to allow a blood product to contact said resin.

55. The method of Claim 54, wherein said second container further comprises an inlet/outlet line.

56. The method of Claim 55, wherein said retaining means comprises a mesh filter positioned in said inlet/oulet line and in fluidic communication with said biocompatible housing.